# COMPARATIVE STUDY OF CAROTID INTIMA MEDIA THICKNESS IN ISCHEMIC STROKE SUBTYPES

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## ABSTRACT

Ischemic stroke is a heterogeneous disease, with different subtypes, each of them presenting specific etiopathogenic aspects in which atherosclerosis and small vessel disease play a crucial role. Increased common carotid artery intima-media thickness (IMT) is a marker of atherosclerosis associated with ischemic stroke.

**Purpose.** The aim of this study was to investigate if increased carotid IMT is related with certain ischemic stroke subtypes according to TOAST and Bamford/Oxfordshire criteria.

**Methods.** In a prospective study 430 patients with ischemic stroke, classified in subtypes according to TOAST and Bamford/Oxfordshire criteria, were evaluated by cervical ultrasound. We measured carotid IMT bilaterally by B mode ultrasound aiming to find a statistical correlation between carotid IMT and stroke subtypes.

**Results.** All 430 patients with ischemic stroke (average age 64,67 years) were divided according to TOAST criteria as follows: 136 (31,63%) LAA, 48 (11,16%) CE, 107 (24,88%) SAA, 6 (1,4%) OE and 133 (30,93%) UE. In these patients mean ipsilateral carotid IMT varied as follows: 1,1426 mm for LAA, 1,0313 mm for CE, 1,0402 mm for SAA, 1,0167 mm for OE and 1,0647 mm for UE, with high statistical significance ($p < 0,00001$). According to Bamford/Oxfordshire classification the distribution of patients was as follows: 121 (28,14%) TACI, 199 (46,28%) PACI, 85 (19,77%) LACI and 25 (5,81%) POCI. In these patients mean ipsilateral carotid IMT varied as follows: 1,124 mm for TACI, 1,0955 mm for PACI, 1,0430 mm for LACI, 1,0776 mm for POCI with lower statistical significance ($p < 0,05$).

**Conclusions.** Highest carotid IMT value was found in LAA, respectively TACI stroke subtypes, and lowest value in SAA, respectively LACI subtypes. High carotid IMT, implicitly atherosclerosis, was better correlated with ischemic stroke due to large vessel disease and less correlated with small vessel disease.

**Key words:** atherosclerosis, ischemic stroke, intima media thickness, stroke subtypes

## INTRODUCTION

Stroke represents one of the leading causes of morbidity and mortality worldwide. Despite all therapeutic advances, primary prevention is still a highly efficient strategy (1).

Ischemic stroke is classified according to various criteria, stroke subtype decisively influencing patient prognosis and evolution (1). Bamford/Oxfordshire classification includes the clinical and imaging aspects (vascular territorial distribution) of stroke (2). TOAST criteria include various etiological, pathophysiological and imaging aspects, while remaining compact and flexible (2,3).

Atherosclerosis, through its complications, is the leading cause of ischemic stroke. Carotid artery intima-media thickness (IMT) progression is the first vascular wall damage marker appearing in the process of atherosclerosis (4). Several studies have demonstrated a higher carotid IMT in patients with nonlacunar versus lacunar stroke (5,6). Other studies did not find any differences (7,8,9).

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The significance of an increased carotid IMT in patients with vascular risk factors is still a matter of debate. At the moment there is no consensus opinion regarding the predictive role of increased carotid IMT in the occurrence of certain ischemic stroke subtypes.

## PURPOSE

In this study we have analyzed mean carotid IMT values in different stroke subtypes according to TOAST and Bamford/Oxfordshire criteria, aiming to find significant correlations between them. We expected to find an increased carotid IMT in ischemic stroke subtypes due to atherosclerosis. Finding such a correlation might reveal the importance of carotid IMT evaluation in primary and secondary prevention of certain ischemic stroke subtypes.

The fact that in Romania there is no large study to assess the specific incidence of stroke subtypes for this region was another reason to make this study.

## SUBJECTS AND METHODS

We made a prospective study on 430 patients with supratentorial ischemic stroke admitted in the Neurology Department of Academic Emergency Hospital Sibiu between 01.01.2008 – 31.12.2009 to which we performed cervical ultrasound.

The presence on admission with characteristic symptoms of supratentorial ischemic stroke confirmed by brain CT or MRI, cervical ultrasound with analysis of common carotid artery IMT and the informed consent of the patient were the study admission criteria. Patients without imagistic confirmation of stroke and those without carotid artery ultrasound examination were excluded from the study.

Based on the evaluation of pathophysiological, etiological and imagistic aspects, patients were divided in 5 categories according to TOAST criteria: LAA = large artery atherosclerosis, SAA = small artery occlusion, CE = cardioembolism, OE = stroke of other determined etiology, UE = stroke of undetermined etiology.

Based on the clinical and imagistic data, patients were divided in 4 categories according to Bamford/Oxfordshire classification of ischemic stroke: TACI = total anterior circulation stroke, PACI = partial anterior circulation stroke, LACI = lacunar stroke, POCI = posterior circulation stroke.

Carotid artery ultrasound examination was made with the ESAOTE MYLAB 50 ultrasonograph in B mode using a 7,5 MHz PW linear probe. Carotid IMT was measured according to current rules in common carotid artery ipsilateral and contralateral related to stroke laterality, in atherom plaques free areas. The value used in the study was the average of 3 measurements in 3 distinct areas with the greatest thickness. Values above 1,49 mm were considered atherom plaques.

Statistical processing was made with IBM SPSS Statistics 19 version. The differences between mean IMT in stroke subtypes were calculated using linear regression analysis. Chi Square test was used to compare IMT progression in our study with the progression appeared as a result of chance.

## RESULTS

The study population consisted of 430 ischemic stroke patients, aged between 35 to 89 years (mean age was 64,67 years). 253 patients (58,84%) were male and 177 patients were female (41,16%), male:female report being approximately 1,5:1.

Patient distribution on TOAST and Bamford/Oxfordshire ischemic stroke subtypes, demographic data and mean ipsilateral and contralateral IMT values on each stroke subtype are presented in Table 1 and Table 2.

Mean ipsilateral IMT was highest in patients with LAA stroke subtype (1,1426 mm), according to TOAST criteriaand in patients with both TACI and PACI subtypes (1,124 mm, respectively 1,0955 mm) in Bamford/Oxfordshire classification.

Mean ipsilateral IMT was lowest in patients with SAA stroke subtype (1,0402 mm), according to TOAST criteria, and in patients with LACI subtype (1,0430 mm) in Bamford/Oxfordshire classification.

IMT values variation related to ischemic stroke subtypes after TOAST criteria (Fig. 1) had high statistical significance ($p < 0,00001$; 95% CI: -0.024 to -0.009).

IMT values variation related to ischemic stroke subtypes in Bamford/Oxfordshire classification (Fig. 2) was at the limit of statistical significance ($p = 0,04$; 95% CI: -0.028 to 0.000).

## DISCUSSION

Increased mean IMT values corresponded to LAA ischemic stroke subtype (TOAST classification) whose pathogenesis is related to large vessel

***TABLE 1.*** *Baseline characteristics of patients with TOAST stroke subtypes*

| | LAA | SAA | CE | OE | UE | p-value |
|---|---|---|---|---|---|---|
| No. of patients (%) | 136 (31,6) | 107 (24,9) | 48 (11,2) | 6 (1,4) | 133 (30,9) | |
| Mean age, y | 67,65 | 68,66 | 61,64 | 52,16 | 63,19 | |
| Male/female (ratio) | 1,7/1 | 1/1,4 | 1,6/1 | 2/1 | 1,4/1 | |
| Mean IMT ipsilateral (mm) | 1,1426 | 1,0402 | 1,0313 | 1,0167 | 1,0647 | <0,00001 |
| Mean IMT controlateral (mm) | 1,1272 | 1,0336 | 1,0229 | 1 | 1,0571 | <0,00001 |

***TABLE 2.*** *Baseline characteristics of patients with Bamford stroke subtypes*

| | TACI | PACI | LACI | POCI | p-value |
|---|---|---|---|---|---|
| No. of patients (%) | 121 (28,1) | 199 (46,3) | 85 (19,8) | 25 (5,8) | |
| Mean age, y | 65,32 | 66,55 | 62,47 | 63,23 | |
| Male/female (ratio) | 1/1,08 | 1,4/1 | 1,5/1 | 1,5/1 | |
| Mean IMT ipsilateral (mm) | 1,124 | 1,0955 | 1,0430 | 1,0776 | 0,04 |
| Mean IMT controlateral (mm) | 1,096 | 1,0864 | 1,0364 | 1,0659 | 0,033 |

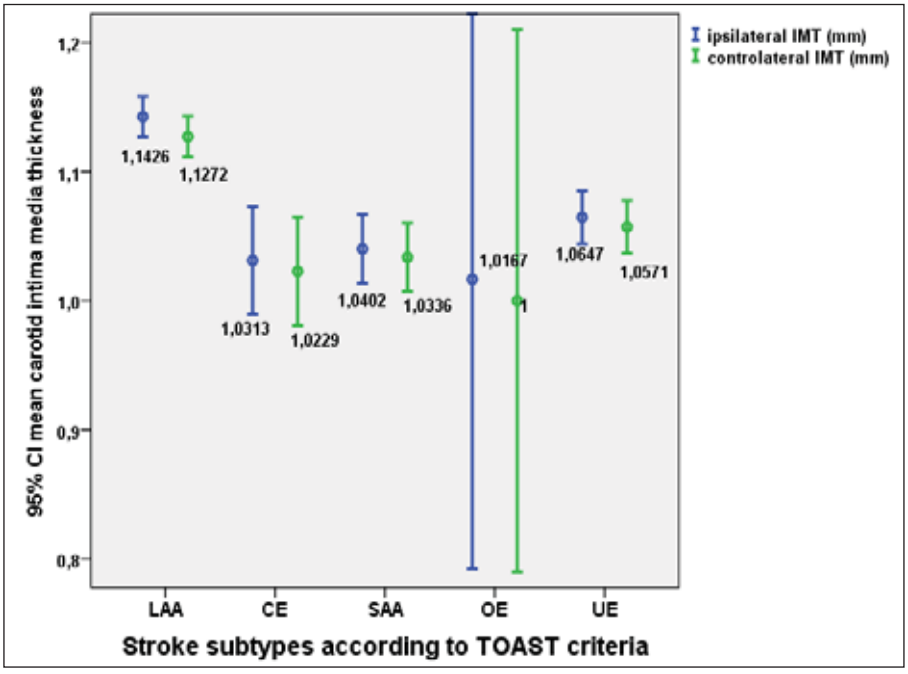


***FIGURE 1.*** *Mean IMT value in TOAST stroke subtypes (LAA = large artery atherosclerosis, SAA = small artery occlusion, CE = cardioembolism, OE = stroke of other determined etiology, UE = stroke of undetermined etiology)*

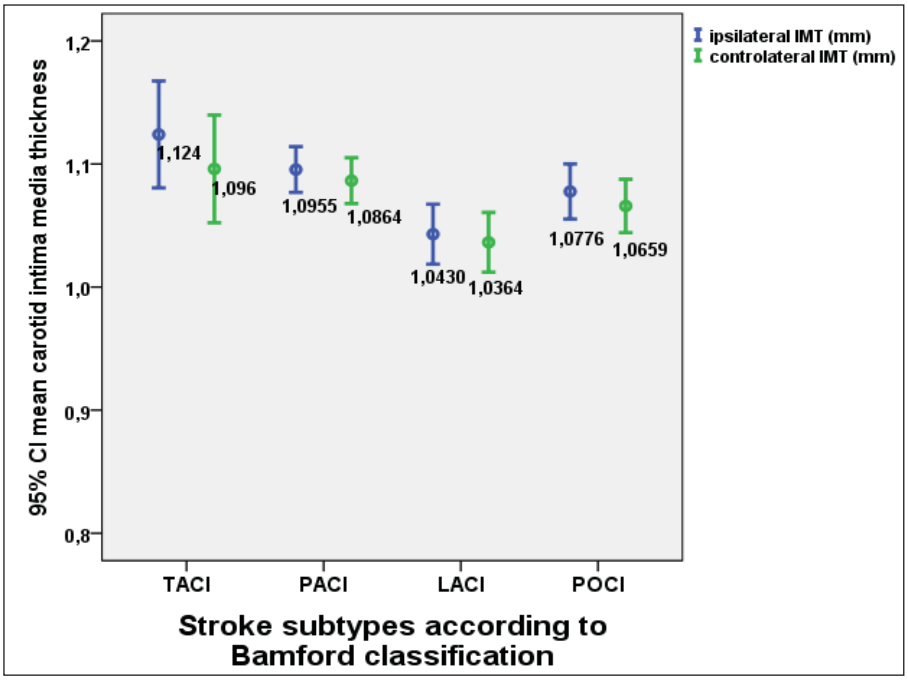


***FIGURE 2.*** *Mean IMT value in Bamford/Oxfordshire stroke subtypes (TACI = total anterior circulation stroke, PACI = partial anterior circulation stroke, LACI = lacunar stroke, POCI = posterior circulation stroke).*

***TABLE 3.*** *Review of previous studies*

| | Touboul et al[7] | Cupini et al[5] | Nagai et al[8] | Pruissen et al[6] | Our study |
|---|---|---|---|---|---|
| No. of patients | 207 | 192 | 185 | 532 | 430 |
| Mean age, y | 65 | 70,3 | 64 | ≈62 | 64,67 |
| Mean IMT in SVD (mm) | 0,80 | 0,91 | 0,91 | 0,92 | 1,04 |
| Mean IMT in LVD (mm) | 0,83 | 1,04 | 0,92 | 1,08 | 1,14 |
| Subtype classification system | Own criteria | TOAST | Own criteria | Own criteria | TOAST, Bamford |

disease and to TACI and PACI subtypes (Bamford classification) whose pathogenesis can be equally due to atherosclerosis and cardioembolism. SAA and LACI ischemic stroke subtypes which are secondary to small vessel disease have lessen mean IMT values. These results correspond to data obtained in two previous studies (5,6). There are three previous studies that found no significant differences between carotid IMT values in lacunar versus non-lacunar infarcts (7,8,9). The values published in those studies are summarized in Table 3.

The lowest mean IMT values (1,03 mm) were found in patients with CE subtype, likely due to the 6 years lower mean age compared to the other stroke subtypes and its different pathogenesis.

Due to the fact that TOAST is a pathophysiological/etiological classification, we expected to find a high correlation between LAA stroke subtype and increased carotid IMT. On the other hand, Bamford/Oxfordshire being a clinical and anatomical classification whose subtypes have different etiologic mechanisms, the correlation with increased carotid IMT was at the limit of statistical significance and has no practical value. Thisuselessnessof Bamford/Oxfordshire classification was also mentioned by Amarenco in 2009 (2).

Mean IMT values of the patients in our study are approximately 0,1 mm higher than the mean IMT reported in previous studies, while the mean age is roughly similar (Table 3) (5,6,7,8). These data suggest that atherosclerosis progression is higher to the population in our geographic area, specific vascular risk factors and health services probably contributing to this evolution. It is known that life expectancy in Romania is about 10 years less as in Western Europe.

Mean IMT value was higherin stroke ipsilateral common carotid artery compared to contralateral common carotid artery.

## CONCLUSIONS

The association between IMT values and ischemic stroke subtypes had high statistical significance in TOAST classification ($p < 0,00001$; Chi Square test $p < 0,0001$) and a borderline and doubtful statistical significance in Bamford/Oxfordshire classification ($p = 0,04$; Chi Square test $p < 0,05$), increased mean IMT values correlating better with ischemic stroke consecutive to large vessel disease and less with lacunar infarcts.

Our study reveals the importance of carotid IMT evaluation at the patients with atherosclerotic risk factors and suggests a predictive role of increased carotid IMT for ischemic stroke subtypes related to large vessel disease. Future research on this matter could lead to a more efficient primary prevention of these ischemic stroke subtypes.

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